

## II. *On the Secretion of Saliva, chiefly on the Secretion of Salts in it.*

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### PREVIOUS OBSERVATIONS.

THE earliest observations on variations in percentage of salts in saliva with which we are acquainted, are those of LUDWIG and BECHER,\* in 1851. They analysed successive portions of saliva, obtained under different conditions, from the submaxillary gland of the Dog.

Three experiments were made on the effect of protracted secretion ; in two of these the percentage of salts sank in the successive portions of saliva, but in the remaining one, the third and fourth samples of saliva contained a rather higher percentage of salts than the second and first samples. The total amount of saliva collected in this case was 48·5 grm.

Three experiments were made in the following manner :—Saliva was collected, then blood withdrawn from the animal, water injected in the place of the blood, and saliva again collected ; in two of these experiments the defibrinated blood was re-injected, and a further portion of saliva obtained. In all these cases the percentage of salts in the saliva sank during secretion.

Lastly, in one experiment fourteen samples of saliva were obtained, in all 177 grm. ; and twice during the course of the experiment 150 grm. of a 7·33 per cent. solution of sodium chloride were injected. After the first injection there was a rise in the percentage of salts in the saliva ; after the second injection there was a fall in the percentage of salts below that of the first sample. A few only of the samples of saliva were analysed.

These observations showed that during secretion the percentage of salts falls in most, but not in all, cases ; and they indicated that the percentage of salts depends upon the condition of the gland with regard to fatigue.

HEIDENHAIN† placed the matter on a different basis. He analysed successive small quantities of saliva, secreted at different rates, and found that, up to a certain limit,

\* LUDWIG and BECHER, 'Zeitschr. f. rat. Med.,' New Series, vol. 2, 1851, p. 278.

† HEIDENHAIN, 'Studien des physiol. Instituts zu Breslau,' Part 4, 1868, pp. 30 *et. seq.*, and 'Archiv f. d. gesammte Physiologie,' vol. 17, 1878, p. 3.

the percentage of salts in saliva increases with its rate of secretion. As we shall frequently have occasion to refer to this conclusion, we shall, for the sake of brevity, call it HEIDENHAIN'S law.

Since, in experiments like those of LUDWIG and BECHER, the rate of flow of saliva would, as a rule, steadily decrease, it was most probable that the variations in the percentage of salts observed by them were due to variations in the rate of secretion. And HEIDENHAIN\* came to the conclusion that the percentage of salts in saliva was not influenced by the state of the gland, except in so far as the state of the gland led to an alteration in the rate of flow; so that at the end of a protracted secretion, the percentage of salts would be the same as at the beginning, provided the rate of secretion were the same.

WERTHER,† in the course of some observations on the secretion of the various salts which occur in saliva, has repeated HEIDENHAIN'S experiments, taking larger quantities of saliva, and confirms HEIDENHAIN'S conclusions.

So far, then, it would appear that the secretion of salts depends in some not clearly definable way upon the secretion of water, and upon that alone.‡

Both in HEIDENHAIN'S and in WERTHER'S Tables there are a considerable number of departures from the law that an increased rate of secretion causes an increased percentage of salts. In HEIDENHAIN'S§ experiments, out of thirty-six estimations there are thirteen divergences from the law. Some of these, it is true, are slight. They are all referred by HEIDENHAIN to unavoidable variations in the rate of secretion during the time of collecting each sample of saliva. But it must be noticed that HEIDENHAIN does not expressly say that he observed during the collection of the samples of saliva any especial variation in the rate of secretion of those particular samples which, on analysis, were found not to follow the law of increased percentage of salts with increased rate of secretion. Hence, although the explanation is a probable one, it is, as matters stand, not satisfactorily proved.

*Causes of Variation in the Rate of Secretion, on apparently Equal Stimulation of the Chorda Tympani.*

In order to observe accurately the connection between the rate of secretion and the percentage of salts in the saliva, it is essential that each sample of saliva should be secreted at the same rate throughout. It is, however, impossible, except in very large Dogs, to obtain a sufficient quantity of saliva for analysis, the rate of secretion

\* HEIDENHAIN, *op. cit.*, 1878.

† WERTHER, 'Archiv f. d. ges. Physiologie,' vol. 38, 1886, p. 293.

‡ It was some time ago pointed out by one of us ('Journal of Physiology,' vol. 2, p. 269, 1879) that the percentage of salts in saliva does not always increase with an increase in the rate of secretion. But the only analyses given were of parotid saliva in the Dog, obtained first by stimulating the sympathetic, and then by injecting pilocarpin. For an account of the recent observations of NOVI, *cf.* p. 150.

§ 'Archiv f. d. ges. Physiologie,' vol. 17, p. 8, Table II.

of which is constant. During the time of collecting the saliva the rate of secretion varies; in two successive samples the variation in rate will almost certainly be not quite the same, and, in consequence, the relation between the percentage of salts and the rate of secretion will be obscured. The variations in the rate of secretion which occur when the chorda tympani is stimulated are partly due to normal causes, and partly to abnormal causes brought about by the exposure of the nerve. Normally, when the chorda tympani is stimulated the rate of secretion rapidly rises to a maximum, and then slowly declines. When the nerve is dissected out, its irritability gradually falls, and if, as often is the case in dissecting out the chorda, some lobules of the sub-lingual gland are cut through, so that their secretion oozes out and soaks into the nerve, its irritability falls rapidly; in either case it may happen that, in collecting a sample of saliva, the stimulus previously causing a rapid secretion causes only a slow one; on seeking to correct this by increasing the strength of the stimulus the secretion often becomes over-rapid, and a mixture of salivas secreted at very different rates is the result.

Further, as HEIDENHAIN has pointed out, a variation in rate is brought out on chorda stimulation by the unequal irritability of the nerve along its course; a very slight shifting of the electrodes in either direction may cause a considerable variation in the rate of secretion. In Experiment 2, No. I., for example, the electrodes were placed on the part of the chorda adjoining the lingual nerve, but the number of drops of saliva produced by stimulating for 30 seconds varied from 1 to 4 with the index of the secondary coil at 12 cm., and from  $3\frac{1}{2}$  to 8 with the index of the secondary coil at 11.5 cm.

#### VARIATIONS IN THE PERCENTAGE OF SALTS IN CHORDA SALIVA OBTAINED UNDER NORMAL CONDITIONS.

Our first experiments were to try whether, by noting the variations in the rate of secretion during the time of collecting each sample of saliva, we could account for any variation that might occur in the percentage of salts. But, as we had no doubt of the general truth of HEIDENHAIN's conclusions, we performed the experiments under somewhat different conditions from those of HEIDENHAIN, so as to still further test these conclusions.

*Unless otherwise mentioned the following procedure was adopted in each of the Experiments.*

Morphia in 5 per cent. solution was injected sub-cutaneously; in half to three-quarters of an hour, when severe pinching of the skin produced no movement, the animal was given chloroform. A three-way tube was tied in the trachea, one limb of the tube being connected at intervals with a bottle containing a mixture of chloroform and ether.

The lingual nerve was ligatured and cut peripherally of the point where it gives off the chorda tympani; lifting this up, the central end of the lingual nerve and then the chordo-lingual were isolated

for some little distance, the chordo-lingual cut, and the chorda tympani isolated for a variable distance. During stimulation the lingual nerve was raised by the ligature, and the electrodes slipped under the chorda; in the intervals of stimulation the chorda was covered up.

The interrupted current of a du Bois' induction machine was used for stimulation; in the account of the experiments, the distance of the index of the secondary coil from the primary is given in centimetres; thus,  $c = 12.5$  indicates that the index of the secondary coil was at 12.5 cm. of the scale attached to the machine. One Daniell's cell was used, but not the same in the several experiments.

A glass cannula was tied in WHARTON'S duct, and, for convenience of collecting the saliva and of counting the drops, the cannula was bent at the end. The object of counting the drops was to note variations in the rate of secretion whilst collecting any one sample of saliva; since the size of the drops depends upon the rate of secretion and upon various other conditions, the number of drops collected in successive samples often gives a very rough indication only of the amount of saliva in each.

The saliva was collected in small-necked bottles graduated in centimetres, so that the amount of saliva obtained at any time could be roughly estimated. The saliva was measured in the following way:—The level of the saliva in the bottle was marked by a strip of adhesive paper, the bottle was emptied and dried, and then water was allowed to run into it from a burette up to the level of the strip of paper.

*Before collecting a sample of saliva under any given conditions, 1 to 3 c.c. of saliva obtained under these conditions were thrown away.*—In the account of the several experiments the amount thrown away is, for special reasons, occasionally mentioned, and always when the amount thrown away was less than .75 c.c. It may be mentioned that one to two drops is probably as much as the gland ducts and lumina contain.

The sympathetic nerve, when it was necessary to stimulate it, was dissected out from the vagus in the neck, ligatured, and cut. When salt solution or other fluid in quantity was injected into the blood it was first warmed to about 38° C.

Pilocarpin was injected into the blood as pilocarpin nitrate, and atropin as atropin sulphate.

*Method of Analysis.*—The amount of each sample of saliva collected is given in the description of the experiments. When there was sufficient saliva, 2.8 to 3.0 c.c. were taken for analysis. The weighed quantity of saliva was dried in a platinum crucible at 100° C. This temperature was found to be quite high enough to drive off all the water in five to six hours. When further heating of the crucible produced no diminution in weight, the weight of the residue, after cooling over sulphuric acid, gave the total amount of solids. The residue was then carefully ignited over a Bunsen flame, the crucible being held in the flame by means of tongs. The smallest possible amount of heat necessary to secure complete ignition of the organic compounds was employed, in order to prevent loss by volatilisation and possible loss by some of the fused salts creeping over the edge of the crucible. Less than three-quarters of a minute generally sufficed to burn off all carbonaceous matter. The residue, weighed after cooling over sulphuric acid, gave the total salts. The weighing was performed to .0001 grm. In the Tables we have given the percentage composition of the various samples of saliva to three places of decimals only, since, for our purposes, the inaccuracy incidental to the determination of the rate of secretion made of no value the fourth—and sometimes the third—place of decimals in the percentage composition.

*Experiment 1.*

July 29, 1887. Dog, rather small. The saliva in each case was obtained by stimulating the chorda tympani.

Number of sample.	Time of beginning to collect saliva.	Position of secondary coil.	Total time of collection of saliva in minutes.	Amount of saliva, and time during which actually secreted.	Rate of secretion in c.c. per min.	Mean rate of secretion.	Percentage of organic substance.	Percentage of salts.	Remarks.
I.	11.46	17	7½	1 c.c. in 2 min. 4 c.c. in 4½ min.	.5 .9	.770	1.722	.595	Chorda was stimulated twice, interval of 1 min. between the stimulations. Probably owing to a slight difference in the position of the electrodes, the secretion was much faster during the second stimulation.
II.	12.8	8.5	3	4 c.c. in 3 min.	1.333	1.333	1.433	.628	Secretion continuous.
III.	12.43	17 16	7½	.7 c.c. in 3½ min. 4.8 c.c. in 4 min.	.200 1.200	.733	1.214	.651	Secretion slow with $c = 17$ , alter to $c = 16$ secretion becomes rapid, towards end of time less rapid.
IV.	1.0	8.5	7	1.8 c.c. in 2 min. 2.5 c.c. in 5 min.	.900 .500	.614	.738	.553	Secretion decreases in rate after first two minutes.
V.	1.20	16—15	14	3.6 c.c. in 9 min.	.400	.400	.707	.472	Chorda stimulated three times, with intervals of rest.
VI.	1.47	16	6½	3.8 c.c. in 5 min.	.760	.760	.584	.599	Chorda stimulated five times, with intervals of rest.

If we take here the mean rate of secretion, we see that there are several divergences from HEIDENHAIN's law ; of these I. and VI. can be explained by taking into consideration the variation in the rate of secretion during the time of collecting I. In I. the 4 c.c. of the saliva collected is secreted at a rate of .9 c.c. a minute, and 1 c.c. at a rate of .5 c.c. a minute. In V. the percentage of salt is .472 in saliva secreted at a rate of .400 c.c. a minute, so that, allowing an increase of .004 per cent. for each .01 c.c. increase in rate, the percentage of salts in saliva secreted at a rate of .5 c.c. a minute would be .512. Hence, the saliva in I., secreted at a rate of .9 c.c. a minute, contains .616 per cent. of salts, *i.e.*, a higher percentage of salts than sample VI.

On the other hand, the difference in the percentage of salts between II. and III. cannot be altogether satisfactorily explained in this manner. The saliva III., secreted at a slower rate than II., should have a lower percentage of salts ; in fact, the percentage of salts in it is higher. It is true that a portion of III. may have been secreted at a faster rate than any in II., for in III. 4.8 c.c. were secreted at a mean rate of 1.2 c.c., and, as the rate of secretion slackened towards the end of stimulation, the rate was, of course, considerably faster than 1.2 c.c. a minute at the beginning of the stimulation ; but, in view of the slight increase in the percentage of salts which occurs as the rate of saliva approaches its maximum (*cf.* p. 117), this explanation is insufficient. It is possible that the increased percentage of salts may have been due to the blood-flow through the gland being in this case less than normal (*cf.* p. 126).

In the experiment given above, the stimulation of the chorda tympani was, in most cases, stopped as soon as the secretion, beginning fairly rapidly, began to be obviously slower. In the following experiment, a variation of this procedure was made by stimulating the chorda for a definite short portion of each minute, so that the stimulus ceased at about the period of the maximum rate of secretion for the stimulus used. With both methods, there is usually a small amount of saliva secreted slowly, after the stimulation of the nerve has ceased.



In this experiment, the percentage of salts follows HEIDENHAIN'S law in all five cases, and does so *although the slower secretions were obtained by stimuli so strong as to rapidly exhaust the irritability of the nerve, instead of by weak stimuli*. This, taken with Experiment 1, in which, out of six cases, there was but one exception to the law, and that a not very certain one, is strong confirmation of HEIDENHAIN'S suggestion that the exceptions found in his experiments are due to variations in the rate of flow of saliva during the time of collecting any one sample.

In all these cases, the saliva is obtained by stimulating the chorda tympani, under normal conditions of blood supply, except that curari or an anæsthetic in sufficient, but not in excessive, amount may have been given; as we shall see later, under other conditions the percentage of salts does not necessarily increase with the rate of secretion of the saliva. Before considering what these conditions are, we may say a word or two about the relation between the increase of flow of saliva and the rate of increase of the percentage of the salts.

HEIDENHAIN (*op. cit.*, p. 9) states that, with increasing rate of secretion, the percentage of salts increases up to a maximum of  $\cdot 5$  to  $\cdot 6$  per cent., so that his law really only holds within certain limits; when the rate of secretion passes a certain limit—variable in different glands—the percentage of salts in the saliva no longer increases. WERTHER points out that the highest percentage of salts given by HEIDENHAIN for sub-maxillary saliva is  $\cdot 66$  per cent., whilst in his own experiments the maximum is  $\cdot 77$  per cent. In our experiments the maximum percentage of salts is also  $\cdot 77$  per cent. (*cf.* p. 122, Table VI.). LUDWIG and BECHER in one case found  $\cdot 78$  per cent. of salts.

We do not think that there is any satisfactory proof that under normal conditions of blood flow, and with saliva obtained by stimulating the chorda tympani, there is any upper limit in the rate of secretion beyond which an increase in rate no longer produces an increase in the percentage of salts.

In Experiment 2, three of the samples of saliva are secreted at a fairly constant rate, and under similar conditions are:—

TABLE I.

	Rate of secretion per minute in c.c.	Percentage of salts.
IV.	$\cdot 400$	$\cdot 598$
V.	$\cdot 455$	$\cdot 626$
III.	$\cdot 525$	$\cdot 652$

Comparing IV. and V., we see that an increase in rate of  $\cdot 055$  c.c. a minute gives an increase in the percentage of salts of  $\cdot 028$  c.c.; the rate of increase is about  $\cdot 0051$  per cent. of salts for  $\cdot 01$  c.c. a minute of saliva.

Comparing V. and III., we see that an increase in rate of secretion of  $\cdot 089$  c.c. a



minute gives an increase in the percentage of salts of  $\cdot 026$  per cent., *i.e.*, the rate of increase is about  $\cdot 0037$  per cent. of salts for  $\cdot 01$  c.c. a minute of saliva.

Here the first increase in the rate of secretion produces a greater proportional increase in the percentage of salts than does the subsequent additional increase in the rate of secretion.

Taking similarly from Experiment 1 the three samples of saliva which were secreted with the least variation in rate during the collection of each sample, we have :—

TABLE II.

	Rate of secretion per minute in c.c.	Percentage of salts.	Increase in percentage of salts corre- sponding to an increase of $\cdot 01$ c.c. per minute in rate of secretion.
V.	$\cdot 400$	$\cdot 472$ }	$\cdot 0035$
VI.	$\cdot 760$	$\cdot 599$ }	
III.	$1\cdot 333$	$\cdot 628$ }	$\cdot 0005$

or inserting the calculated rates from I. and IV. :—

TABLE III.

	Rate of secretion per minute in c.c.	Percentage of salts.	Increase in percentage of salts corre- sponding to an increase of $\cdot 01$ c.c. per minute in rate of secretion.
V.	$\cdot 400$	$\cdot 472$ }	$\cdot 004$
I <sub>a</sub> .	$\cdot 500$	$\cdot 512$ }	
VI.	$\cdot 760$	$\cdot 599$ }	$\cdot 0033$
I <sub>b</sub> .	$\cdot 900$	$\cdot 616$ }	$\cdot 0012$
III.	$1\cdot 333$	$\cdot 628$ }	$\cdot 0003$

We conclude then that the percentage of salts in saliva increases as long as the rate of secretion increases, but that the increment in the percentage of salts becomes less with each successive equal increment in the rate of secretion.

We may now pass to consider the conditions under which the statement just made no longer holds.

## EFFECT OF STIMULATING THE SYMPATHETIC NERVE.

As far as we know, no attention has been called to the fact that the percentage of salts in sympathetic saliva is greater than that which corresponds to its rate of secretion, if chorda saliva be taken as a basis of comparison.

The following experiments bring out clearly the lack of correspondence between the rate of flow and the percentage of salts, when sympathetic and chorda saliva are compared:—

*Experiment 3.*

August 5, 1887.—Dog. Weight,  $5\frac{1}{4}$  kilos. Cannula in right sub-maxillary duct. Cannula for injection in left jugular vein.

2.15. Stimulate chorda,  $c = 19$ , no secretion;  $c = 18$ , fairly copious viscid secretion.

2.25. Stimulate sympathetic,  $c = 8$ , very slow secretion.

2.47 $\frac{1}{2}$ . Inject 3 mgrm. pilocarpin. Let 25 drops run away, then Collect I. The drops in successive 30 sec. were

4.4.4.4.5.4.4.4.4.3.4.3.3. = 2.6 c.c. in  $6\frac{1}{2}$  min.

3.1 $\frac{1}{2}$ . Stimulate sympathetic,  $c = 8$  for 3 min. The secretion stops for 5 min. and then begins again, going on at a rate of 1 to 2 drops in 30 sec.

3.11. Inject 3 mgrm. pilocarpin.

3.12. Collect II. Drops in each 30 sec. were

$\frac{1}{2} \cdot \frac{1}{2} \cdot \frac{1}{2} \cdot \frac{1}{2} \cdot 1 \cdot 1 \cdot 1 \cdot 2 \cdot 2 \cdot 2 \cdot 2 \cdot 2 \cdot 0 \cdot 0 \cdot 0 \cdot 1 \cdot \frac{1}{2} \cdot \frac{1}{2} \cdot 3 \cdot 3 \cdot 4 \cdot 1 \cdot \frac{1}{2} \cdot 1 \cdot 2 \cdot 2 \cdot 2 \cdot 2 \cdot 3 \cdot 0 \cdot 1 \cdot 3 \cdot 3$   
 $c = 8 \qquad c = 10 \qquad c = 15$   
 $1 \cdot 2 \cdot 2 = 2.8$  c.c. in 18 min., the actual time of secretion being 16 min.

During the secretion of the drops doubly underlined, the sympathetic was stimulated. During the secretion of the drops singly underlined, the chorda was stimulated for a part of the 30 sec.; this was done chiefly to prevent the complete cessation of the secretion, which the previous trial had shown to be the result of strong stimulation of the sympathetic.

3.30. III. Immediately after collecting II., the collection of saliva in III. was begun; thus the first part of this was saliva secreted previously and of the same nature as that in II. Drops in each 30 sec. were

2.1.1.1.2.3.2.2.3.2.3.2.2.3.2.2.2.3.2.3.2.2.3.2 = 2.6 c.c. in  $12\frac{1}{2}$  min.

3.42 $\frac{1}{2}$ . IV. Saliva collected immediately after the end of the previous collection, so that this saliva contained part of saliva secreted under conditions of III., *i.e.*, from pilocarpin alone. The sympathetic, during the secretion of the underlined drops in the following, was stimulated with *weak* induction shocks,  $c = 25$  to 30 for 15 to 25 sec. The chorda (at beginning of experiment) first gave a secretion with  $c = 18$ .

2.3.0.1.0.0.0.1. $\frac{1}{2}$ . $\frac{1}{2}$ .1.2.2.2.3.1. $\frac{1}{2}$ . $\frac{1}{2}$ .1.2.3. $\frac{1}{2}$ . $\frac{1}{2}$ .2. $\frac{1}{2}$ . $\frac{1}{2}$ .1.2.2.2.2.2.  
 $c = 20 \qquad c = 25 \qquad c = 25 \qquad c = 30$   
 $2 \cdot 1 \cdot 1 \cdot 2 \cdot 1 \cdot 1 \cdot 2 \cdot 1 \cdot 1 \cdot 1 \cdot 1 \cdot 1 \cdot 1 \cdot 1 \cdot 1 \cdot 2 = 3$  c.c. in 24 min.; actual time of secretion  
 $c = 27$   
 22 min.

4.9. After about 6 drops had been allowed to run away, the saliva was again collected, the chorda

being stimulated in alternate periods of 30 sec. for 25 to 30 sec.,  $c = 16$ . The first stimulation was for 15 sec. only. The number of drops secreted in each 30 sec. were

$2 \cdot \frac{3}{4} \cdot 3 \frac{1}{4} \cdot 1 \cdot 3 \cdot 1 \cdot 4 \cdot 1 \cdot 4 \cdot 1 \cdot 4 \cdot 1 \cdot 4 \cdot 1 \cdot 3 \cdot 1 \cdot 4 \cdot 1 \cdot 4 \cdot 1 \cdot 4 \cdot 1 \cdot 3 = 2 \cdot 8$  c.c. in  $11 \frac{1}{2}$  min.

	Time of collecting saliva.	Duration of secretion in min.	Number of c.c. of saliva.	Rate of flow per min. in c.c.	Percentage of organic substance.	Percentage of salts.	Remarks.
I.	2.51 – 2.57 $\frac{1}{2}$	6 $\frac{1}{2}$	2.6	.400	.324	.728	Saliva obtained by injecting 3 mgrm. of pilocarpin.
II.	3.12 – 3.30	16	2.8	.175	1.138	.726	3.11. Inject 3 mgrm. pilocarpin.
III.	3.30 – 3.42 $\frac{1}{2}$	12 $\frac{1}{2}$	2.6	.208	.563	.704	Stimulate sympathetic and chorda occasionally.
IV.	3.42 $\frac{1}{2}$ – 4.6 $\frac{1}{2}$	22	3.0	.136	.463	.711	Weak stimulation of sympathetic. $c = 20$ to 30.
V.	4.9 – 4.20 $\frac{1}{2}$	11 $\frac{1}{2}$	2.8	.243*	.857	.623*	Stimulate chorda. $c = 16$ .

Here pilocarpin produces a fairly rapid secretion, the saliva having a high percentage of salts, viz., .728. Whilst the secretion from pilocarpin is going on but more slowly, the sympathetic is stimulated; the rate of secretion of saliva is reduced from  $\frac{1}{2}$  to  $\frac{2}{3}$ , but the percentage of salts remains nearly the same (.726); the subsequent saliva from pilocarpin alone, although faster, has a less percentage of salts (.704); this is increased by weak stimulation of the sympathetic (.711), although the rate of secretion is considerably decreased, and this is the more noteworthy, since the percentage of organic substance was very little affected by the weak stimulation of the sympathetic. Finally, stimulation of the chorda decreases the percentage of salts, although about doubling the rate of secretion.

The divergence from HEIDENHAIN'S law will perhaps be more easily seen, if II.–V. are arranged in order of rate of secretion.

\* In V. there is a mixture of salivas secreted at different rates, viz., very nearly 2.2 c.c. at a rate of .37 c.c. a minute, and .6 c.c. at a rate of .11 c.c. a minute.

It is most unlikely that a difference in rate of .01 c.c. a minute could cause here a greater difference in percentage of salts than .01. If we take this as being the true relation, we have

	Rate of secretion per minute in c.c.	Percentage of salts.
V <sub>a</sub> .	.37	.679
V <sub>b</sub> .	.11	.419

TABLE V.

	Rate of secretion per minute in c.c.	Percentage of salts.
V.	·370	·679 about*
III.	·208	·704
II.	·175	·726
IV.	·136	·711

It will be observed that the experimental errors are such as to make the contrast less striking, for, by admixture of some saliva II. with saliva III., the percentage of salts in III. is too high; and by admixture of saliva III. with saliva IV., the percentage of salts in IV. is too low.

*Experiment 4.*

August 10, 1887.—Rather small Dog.

11.45. Stimulate chorda,  $c = 16$  to  $c = 13$ , no secretion;  $c = 12$ , rapid secretion.

12.5. Collect I. Stimulate chorda for 30 sec. in each minute,  $c = 12$ . Number of drops in each 30 sec. of stimulation were

$$4.4.4.2.7.3.5.5.4 = 2.7 \text{ c.c.}$$

There was a secretion of about half a drop, lasting about 15 sec. after the end of each stimulation, so that 2.3 c.c. were secreted in the  $4\frac{1}{2}$  min. of stimulation, and .4 c.c. in  $2\frac{1}{4}$  min. after the stimulation had ceased.

12.25. Inject 1 c.c. .1 p.c. atropin sulphate into jugular vein.

12.40. Stimulation of the chorda,  $c = 12$  to  $c = 3$ , gives no secretion or a mere trace.

Stimulate sympathetic; 7 drops of saliva thrown away.

1.33. Collect II. Stimulate sympathetic as a rule for 30 sec. in each minute,  $c = 8$ . There is a slow secretion which usually continues for 15 or more sec. afterwards. In 139 min., the sympathetic being stimulated altogether for 56 min., 2½ c.c. of saliva are collected. This gives the rate of secretion as .036 c.c. per minute; but, as the saliva continued to flow in the intervals of stimulation, the rate was really slower than this.

4.0. Stimulate chorda, secretion slow, 2 to 3 drops a minute; the amount is proportional to the length of the intervals of rest.

4.6. Collect III. Stimulate chorda,  $c = 8$  in alternate 15 sec. for  $6\frac{1}{2}$  min., then  $c = 8$  to  $c = 6$  for 15 sec. in each 45 sec. for 21 min. *i.e.*, total time of stimulation was  $13\frac{1}{2}$  min. out of 34 min., 2.5 c.c. of saliva were collected; reckoning the time of stimulation only, the rate of secretion is .185 c.c. a minute. This, of course, is a little too high.

4.47. Inject 1.5 c.c. .5 p.c. pilocarpin. Twelve drops thrown away.

4.50. Collect IV. There were 4 drops every 30 sec. for 4 min.; then 3 drops every 30 sec. for  $4\frac{1}{2}$  min.

4.59. Collect V. Drops in each 30 sec., were

$$3.3.3.2.2.2.2.2.2.2.1.1.2.1.2.1.1.2.2.1.1.2.1.1.2.1.1.2.1.1.2.1.$$

5.16½. Inject 1.25 c.c. .5 p.c. pilocarpin. About  $3\frac{1}{2}$  c.c. secreted, then stimulate chorda. Ten drops thrown away.

5.32. Collect VI. Stimulate chorda  $c = 8$  in alternate 30 sec., very little effect on secretion, increasing, perhaps, the continuous secretion by  $\frac{1}{2}$  a drop a minute during the earlier period of collecting; secretion begins 4 and ends  $2\frac{1}{2}$  drops a minute.

\* Cf. note p. 119.

	Total time in min. during which saliva collected.	Time in min. of electrical stimulation.	Amount of saliva collected in c.c.	Rate of secretion per min. in c.c.	Percentage organic substance.	Percentage of salts.	Amount organic substance secreted in 100 min. in grams.	Amount of salts secreted in 100 min. in grams.	Remarks.
I.	12.5	9	2.3 in $4\frac{1}{2}$ ' .4 in $2\frac{1}{4}$ '	.511 .177	1.338	.616	..	..	Stimulate chorda $c = 12$ . 12.25. Inject 1 mgrm. atropin, chorda nearly paralysed.
II.	1.33	139	2.0	.036	1.335	.455	..	..	Stimulate sympathetic.
III.	4.6	34	2.5	.185	.258	.258	.0477	.0477	Stimulate chorda $c = 8$ to $c = 6$ . 4.47. Inject 7.5 mgrm. pilocarpin.
IV.	4.50	8 $\frac{1}{2}$	3.2	.376	.098	.358	.0368	.1346	
V.	4.59	17	3.1	.182	.085	.238	.0154	.0432	5.16. Inject 6 mgrm. pilocarpin.
VI.	5.32	17 $\frac{1}{2}$	3.1	.177	.141	.352	.0249	.0623	Stimulate chorda $c = 8$ , rate of secretion barely affected.

It will be seen in the above experiment that, notwithstanding the very slow rate of secretion of the sympathetic saliva, it contains a higher percentage of salts than five out of the six other samples of saliva collected. Comparing it with sample IV. we see that, whilst it was secreted at one-tenth the rate, it contains  $\cdot 1$  per cent. more salts.

In the other samples of saliva, with the exception of VI., the salts follow HEIDENHAIN'S law. The exception we shall have occasion to refer to later (p. 148).

A still more striking instance of the high percentage of salts which may be present in sympathetic saliva, compared with that proper to its rate of secretion, is given in another experiment made by us, the details of which have been already published.\* From this we take the following :—

TABLE VI.

Saliva obtained by—	Rate of secretion per minute in c.c.	Percentage of salts.
Stimulating left chorda before atropin given	4.13	$\cdot 742$
Stimulating left chorda and sympathetic after 15 mgrm. atropin .. .. .	$\cdot 073$	$\cdot 619$
Stimulating right chorda before atropin given	4.200	$\cdot 766$
Stimulating right sympathetic after 15 mgrm. atropin .. .. .	$\cdot 023$	$\cdot 705$

Here, on the right side, the rate of secretion of the chorda saliva is about 180 times that of the sympathetic saliva, but it contains only  $\cdot 056$  per cent. more salts.

It will be noticed that, on the left side, the sympathetic saliva has  $\cdot 123$  per cent. less salts than the chorda saliva; whilst, on the right side, the sympathetic saliva has only  $\cdot 061$  per cent. less salts than the chorda saliva, *i.e.*, the fall in the percentage of salts is greater on the side on which the sympathetic saliva is more rapidly secreted. It is, however, just possible that this might have been due to a slight admixture of chorda saliva.

The chief point, however, with which we are concerned is that, when chorda saliva is taken as a standard, the percentage of salts in sympathetic saliva is much higher than that which corresponds to its rate of secretion.

In view of this fact, and of the fact that stimulating the sympathetic nerve causes a very great diminution in the amount of blood flowing through the gland, and in consequence a very great diminution in the supply of oxygen to the secretory cells, the possibility was suggested that if, in other ways, either the blood flow through the gland or the oxygen in the blood were diminished, the percentage of salts in saliva might be increased. We accordingly made some observations on these points.

\* LANGLEY, 'Journal of Physiology,' vol. 9, 1888, p. 59.

## EFFECT OF DYSPNOEA.

*Experiment 5a.\**

Jan. 16, 1888. Dog, weight 29 kilos. Sympathetic nerve uncut. The saliva in each case was obtained by stimulating the chorda,  $c = 14$ . The saliva was secreted fairly rapidly, so that the requisite amount was obtained with a single stimulation.

	Time during which saliva collected in minutes.	Number of c.c. of saliva.	Rate of secretion per min. in c.c.	Percentage of organic substance.	Percentage of salts.	Amount of organic substance in 100 minutes in grams.	Amount of salts in 100 minutes in grams.	Remarks.
I.	12.37	2.7	1.80	1.203	.486	2.1654	.8748	{ 12.39.30 Clamp trachea tubes. 12.40.10 Stimulate chorda, saliva not collected. 12.41.0 Begin collecting saliva II. 12.42.30 End of collection of saliva and of stimulation. Unclamp trachea tubes. { Dyspnoea produced as in II.; no saliva was thrown away between collecting IV. and V. Secretion, rapid at first, became slow towards end.
II.	12.41	2.2	1.47	1.193	.515	1.7537	.7570	
III.	12.49	2.6	1.73	1.174	.487	2.0310	.8425	
IV.	12.55	2.4	1.60	.969	.558	1.5504	.8928	
V.	12.56½	1.6	.80	.942	.390	.7536	.3120	
VI.	1.10	2.1	1.40	.854	.430	1.1956	.6720	

\* The remainder of this experiment is given on p. 135.

In this experiment dyspnoea reduces the rate of secretion of water, but, except when it is prolonged (V.), does not do so to any great degree.

Its chief effect is on the secretion of salts; in II. and in IV., although the rate of secretion of saliva falls, the percentage of salts rises. The *rate* of secretion of salts is diminished in II., but is increased in IV.; in the latter case the rate of secretion of water is very slightly diminished, so that the increase in the rate of secretion of salts may have been due to an increase in the strength of the stimulus caused by a shifting of the electrodes on the chorda tympani. At any rate, when the rate of secretion of water is diminished to a greater extent, as in II. and as in Experiment 6, the rate of secretion of salts falls.

The rate of secretion of organic substance also falls; that this is not solely due to a progressive exhaustion of the gland is indicated by the rate of secretion of organic substance being greater in III. than in II. The percentage of organic substance falls in each successive sample of saliva secreted; with a constant stimulus this is observed normally. But here the drop in the percentage of organic substance does not take place regularly; the more dyspnoea decreases the rate of secretion of water, the less is the drop in the percentage of organic substance, that is to say, dyspnoea decreases the rate of secretion of water more than it decreases the rate of secretion of organic substance.

#### *Experiment 6.*

Jan. 21, 1888.—Dog. Chloroform. (Morphia was not given in this case.) Trachea connected with bottle of chloroform and ether. Stimulate chorda,  $c = 11$ , secretion very slight; repeat,  $c = 7$ , fairly rapid secretion, obtain about 1 c.c. Whilst collecting saliva for analysis, the secondary coil was in all cases at 7.

- 12.0. I. Stimulate chorda 2 min. 25 sec. Obtain 2 c.c. saliva.
- 12.9½. Empty the cannula. Clamp trachea tube, to produce dyspnoea.
- 12.10. Stimulate chorda for 2 min. Cannula full ( $= \frac{1}{3}$  c.c.), and 8 drops saliva; drops not collected.
- 12.12. II. Stimulate chorda 1½ min.; saliva collected; at end of stimulation unclamp trachea tube.
- 12.17. Clamp trachea tube.
- 12.17½. Stimulate chorda 2 min.; saliva collected; at end of stimulation unclamp trachea tube.
- 12.25. Clamp trachea tube.
- 12.25½. Stimulate chorda 2½ min.; saliva collected; unclamp trachea tube. Add contents cannula to saliva collected. Total amount saliva is 2.5 c.c. The total time of secretion is 6 min. + 1 min. (required to fill the cannula). Stimulate chorda; let 11 drops run away.
- 12.36 } III. Stimulate chorda 2½ min., 2½ min. (secretion is slow towards end of these periods of  
to stimulation) and 45 sec. Total time of secretion is 5¾ min. Saliva collected
- 12.47. } = 2 c.c.
- 12.53 } Stimulate chorda occasionally; let about 50 drops saliva run away. Vago-sympathetic  
to in neck cut.
- 1.58 }



- 2.0 }  
to } IV. Stimulate chorda  $1\frac{1}{2}$ ,  $1\frac{1}{2}$ ,  $1\frac{1}{2}$ , and  $\frac{1}{2}$  min., that is for 5 min.; there were considerable  
2.11 $\frac{1}{2}$ . } variations in the rate of secretion. Saliva collected = 2.6 c.c.
- 2.14 }  
to } Clamp trachea tubes and stimulate chorda (3 times) to obtain saliva during dyspnoea, as  
2.22. } in collecting (II.). Saliva not collected.
- 2.24 V. Clamp trachea tube.
- 2.24 $\frac{1}{2}$ . Stimulate chorda for  $1\frac{1}{2}$  min., then unclamp trachea tube.
- 2.30 } Above repeated four times. Chorda stimulated  $1\frac{1}{2}$ , 1,  $1\frac{1}{4}$ , and  $1\frac{1}{2}$  min. Total time secre-  
2.50. } tion  $6\frac{3}{4}$  min. Saliva collected 3 c.c.
- 2.51 }  
to } Chorda occasionally stimulated; 21 drops thrown away.  
3.9. }
- 3.13 }  
to } VI. Stimulate chorda  $1\frac{1}{2}$ ,  $1\frac{1}{2}$ ,  $1\frac{1}{2}$ , and  $\frac{1}{2}$  min., = 5 min. Saliva collected = 3.2 c.c.  
3.30. }
- Trachea tubes clamped for 2 min.; no spontaneous secretion.

	Time of beginning stimu- lation chorda c=7.	Number c.c. of saliva collected.	Rate of flow of saliva per minute in c.c.	Percentage organic substance.	Percentage of salts.	Remarks.
I.	12.0	2.0	.83	1.827	.654	Dyspnoea.
II.	12.12	2.5	.356	2.102	.657	
III.	12.36	2.0	.348	1.669	.556	
IV.	2.0	2.6	.52	.784	.515	Dyspnoea.
V.	2.24	3.0	.44	.760	.651	
VI.	3.13	3.2	.64	.627	.522	

The rates of flow given for II. to VI. are all a little too high, since the duration of stimulation is here taken as the duration of secretion of saliva. There was usually a secretion of something less than a drop of saliva after the end of each stimulation.

In this experiment dyspnoea produces more marked effects; it reduces the rate of secretion of all the constituents of saliva, and presumably by decreasing the irritability of the gland-cells. But its effect on the various constituents of saliva is unequal; it reduces the rate of secretion of water most, and in consequence the percentage composition of the saliva is altered.

Saliva II., collected during dyspnoea, is secreted at less than half the rate of saliva I., but it has nevertheless an equal percentage of salts, and about .1 per cent. more salts than saliva III., secreted at nearly the same rate. So, also, saliva V., collected during dyspnoea, although secreted distinctly more slowly than salivas IV. and VI., before and after it, has .13 to .14 per cent. more salts.

With regard to the percentage of organic substance, it is in the first case of dyspnoea increased, and in the second decreased, but less than it would otherwise have been.

An example of the effect of dyspnœa, when the saliva is obtained by injecting pilocarpin, is given in Experiment 7.

TABLE VII.

	Rate of secretion per minute, in c.c.	Percentage of organic substance.	Percentage of salts.	Saliva obtained by
VI.	·360	1·547	·529	Pilocarpin and stimulating chorda.
VII.	·250	·446	·474	Pilocarpin.
VIII.	·311	·517	·557	More pilocarpin during dyspnœa.

There is here an increase in the percentage of salts during dyspnœa, but the results are complicated by the earlier procedure in the experiment.

Dyspnœa appears also to have an after-effect, tending to increase the percentage of salts, and possibly also of organic substance, in the saliva subsequently secreted; but this after-effect is not great and soon disappears.

The prominent effect of not too prolonged dyspnœa is that, whilst decreasing the rate of secretion of saliva, it increases the percentage of salts, and tends to increase the percentage of organic substance in the saliva.

#### EFFECT OF CLAMPING THE CAROTID.

When one carotid is clamped, the blood flow through the sub-maxillary gland is, as is well known, not stopped, but simply diminished, the degree of diminution varying in different cases. We have tried the effect of clamping the carotid on the composition of saliva in a few cases only; the effect, however, is marked: *clamping the carotid increases the percentage of salts in saliva both during the period of clamping and for a short time afterwards.*

*Experiment 7.*

July 5, 1888.—Dog. Weight, 11½ kilos.

	Time in min. during which saliva collected.	Number of c.c. of saliva collected.	Rate of secretion in c.c. per min.	Percentage of organic substance.	Percentage of salts.	Remarks.
I.	12.29	3.1	1.550	1.239	.499	Saliva obtained by injecting into vein 4 mgrm. of pilocarpin.
II.	12.33	2.5	.500	.540	.512	Carotid clamped; decreases at once the rate of secretion.
III.	12.44½	1.8	.128	.322	.674	12.58. Inject 2 mgrm. pilocarpin.
IV.	12.59	2.8	.933	.837	.675	Carotid clamped.
V.	1.7½	2.5	.357	1.478	.622	1.5. Inject 2 mgrm. pilocarpin.
VI.	1.18½	1.8	.360	1.547	.529	Chorda stimulated.
VII.	1.22	2.0	.250	.446	.474	Inject 10 mgrm. curari, and 3 mgrm. pilocarpin.
VIII.	1.50	2.8	.311	.517	.557	Dyspnoea by stopping artificial respiration, 3 times.
IX.	2.0½	3.1	.206	.819	.625	Dyspnoea 4 times. Carotid clamped.
X.	2.35	2.0	.125	.746	.442	2.28. Inject 4 mgrm. pilocarpin.
XI.	2.56	2.5	.192	1.120	.476	2.30. Unclamp carotid.
XII.	3.17½	2.2	.116	.984	.424	2.54. Inject 8 mgrm. pilocarpin.
						3.9 Inject 15 mgrm. pilocarpin.

It will be seen on comparing I. and II. that clamping the carotid increases the percentage of salts from .499 to .512, although the rate of secretion falls from 1.55 c.c. to .50 c.c. a minute; so also in IX., clamping the carotid during dyspnoea increases the percentage of salts considerably more than does dyspnoea alone (VIII.).

It will be seen also that clamping the carotid has a very great after-effect; this is, in fact, in III. and V. greater than the effect whilst the carotid is clamped; thus in III., collected after removing the clamp from the carotid, the percentage of salts rises from .512 to .674, whilst the rate of secretion falls from .5 c.c. a minute to .128. That the after-effect is slight on clamping for the third time may have been due to the much longer duration—half-an-hour—of the closure of the carotid.

Clamping the carotid increases also somewhat the percentage of organic substance above that which corresponds to the rate of secretion of saliva (*cf.* VIII. and IX.).

A similar result was obtained in Experiment 8.

TABLE VIII.

Secretion obtained by injecting pilocarpin.

	Rate of secretion per minute in c.c.	Percentage of salts.	Remarks.
I.	.675	.559	Dyspnoea, carotid clamped. Collected 8 min. after unclamping carotid.
II.	.250	.420	
VII.	.333	.660	
VIII.	.417	.572	

#### THE EFFECT OF LOSS OF BLOOD.

The details with regard to this are given on p. 130, together with the effect of injecting dilute salt solution into the blood. It will be seen that bleeding decreases the rate of secretion and increases the percentage of organic substance in the saliva. The rate of secretion of salts falls, but its percentage is greater than that which corresponds to the rate of secretion of the saliva.

#### THE EFFECT OF INJECTING DILUTE SALT SOLUTION INTO THE BLOOD.

When dilute salt solution is injected into the blood, the percentage composition of the blood is, of course, altered. To the eye, the tissues, especially the abdominal viscera, become more flushed, and the veins fuller. According to WORM-MÜLLER and others, increasing the volume of the blood 20 to 50 per cent. by transfusion causes no increase of arterial blood pressure, except for a brief time immediately after

the injection, since the small arteries dilate and all the capillary areas become fuller. We have made no direct observations upon the effect of injecting dilute solutions of sodium chloride into the blood on the circulation through the sub-maxillary gland; in our experiments the injection has been followed by increased vigour of heart beats; since at the same time the amount of blood in the body was increased, we conclude that, both during rest and during secretion, more blood flows through the gland than normal, and that the capillary blood pressure is increased.

We find that *injection of dilute salt solution in moderate quantity increases the rate of secretion of saliva with a given stimulus, the percentage of salts in the saliva rising nearly normally; and that injection of dilute salt solution in larger quantity increases further the rate of secretion with a given stimulus, but in this saliva the percentage of salts rises much less than normally, and may even fall.*

*Experiment 8.*

July 6, 1888. Dog. Weight  $8\frac{1}{2}$  kilos. The pilocarpin nitrate solution is injected into a branch of the right crural vein, the sodium chloride solution into a branch of the left crural vein. Vago-sympathetic and chorda cut.

	Time during which saliva collected in min.	Number of c.c. of saliva.	Rate of secretion per min. in c.c.	Percentage of organic substance.	Percentage of salts.	Remarks.
I.	11.55	2.7	.675	.250	.559	11.52. Inject 3 mgrm. pilocarpin.
II.	12.0	2.5	.250	.221	.420	Rate of secretion falls from 8 to 2 drops a minute. 12.10-12.20. Inject 200 c.c. NaCl .2 per cent.; little, if any, effect on rate of secretion.
III.	12.22	3.3	1.650	.294	.752	12.21. Inject 3 mgrm. pilocarpin.
IV.	12.25	3.0	1.000	.203	.607	
V.	12.33	2.9	.161	.264	.467	12.28-12.32. Inject 100 c.c. NaCl .2 per cent.; no appreciable effect on rate of secretion. Secretion falls from 5 to 1 drop a minute in 10 min., then inject 200 c.c. NaCl .2 per cent.; secretion quickens to 3 drops a minute.
VI.	12.53	3	.867	.598	.621	12.51. Inject 3 mgrm. pilocarpin. Urine is brightish red, from hæmoglobin.
VII.	12.57	3.0	.333	.506	.660	Dyspnoea. Clamp trachea tubes three times, altogether for 6 min.; carotid clamped throughout.
VIII.	1.14	2.5	.417	.389	.572	1.10. Inject 3 mgrm. pilocarpin; causes a slight increase only in rate of secretion.
IX.	1.22	2.8	.215	.905	.566	1.20. Let 160 c.c. blood flow from crural artery.* Inject 3 mgrm. pilocarpin; little, if any, increase in rate of secretion.
X.	1.38	2.8	.233	.464	.502	Secretion equal rate throughout. 1.36-1.38. Inject 150 c.c. NaCl .2 per cent.
XI.	1.56	2.8	.117	.939	.457	1.53. Let 200 c.c. blood flow from crural artery. Inject 3 mgrm. pilocarpin; secretion continues to fall in rate.
XII.	2.28	2.6	.217	.374	.436	2.21. Inject 350 c.c. NaCl .2 per cent.; secretion becomes somewhat faster.

\* After each withdrawal of blood the heart-beat could be but feebly felt through the chest-wall; on injecting salt solution the heart-beat was strongly felt.

Here neither the first injection of 200 c.c. NaCl .2 per cent. into the blood, nor the second of 100 c.c., affected appreciably the slow rate of secretion going on at the time, owing to the previous dose of pilocarpin; but the secretion obtained after the first injection of NaCl solution, by giving more pilocarpin (III. and IV.) was unusually rapid in rate; and it seems to us certain that this was due to the salt solution leading to an increased flow of blood through the gland, during the dilatation of the small arteries brought about by the additional dose of pilocarpin. At the same time, it is possible that after injection of salt solution more pilocarpin passes through the gland in a given time, and so helps to increase the rate of secretion. The percentage of salts increased in III. nearly as much as it would normally have done.

There is some difficulty with regard to the percentage of salts in IV., V. In IV. the percentage of salts decreases more than normal; in V. it decreases less than normal. It is possible that the former was due to a more marked action of the salt solution, and that the latter was due to the breaking up of the red blood corpuscles, which about this time gave rise to hæmoglobinuria; possibly, also, from the same cause, the percentage of salts in VI. was rather higher than normal, taking I. as a standard.

The third injection of .2 per cent. NaCl—200 c.c.—trebles the rate of secretion which was slowly going on owing to the previous injection of pilocarpin. The subsequent saliva (VI.) obtained by injecting more pilocarpin is rapid, and, judging from other experiments, more rapid than it would have been but for the injection of the salt solution.

In the latter part of the experiment, the effect of injecting salt solution is much more obvious; it increases the rate of secretion, and decreases the percentage of organic substance and of salts. Taking the samples VIII. to XII. we have—

TABLE IX.

	Rate of secretion per min. in c.c.	Percentage organic substance.	Percentage of salts.	Amount in grams of organic substance secreted in 100 min.	Amount in grams of salts secreted in 100 min.	Remarks.
VIII.	·417	·389	·572	·162	·239	3 mgrm. pilocarpin injected. After withdrawing 160 c.c. blood, and injecting 3 mgrm. pilocarpin. After injecting 150 c.c. NaCl .2 p.c. After withdrawing 200 c.c. blood, and injecting 3 mgrm. pilocarpin. After injecting 350 c.c. NaCl .2 p.c.
IX.	·215	·905	·566	·195	·122	
X.	·233	·464	·502	·108	·177	
XI.	·117	·939	·457	·110	·053	
XII.	·217	·374	·436	·081	·095	

In X. not only does the percentage of salts decrease with an increased rate of secretion of water, but the actual rate of secretion of salts decreases slightly. The latter is no doubt due to the stimulus being weaker in X. than in IX., owing to a partial elimination of the pilocarpin. In the other cases the rate of secretion of salts increases with the rate of secretion of water.

The *rate* of secretion of organic substance is not much affected by the injection of dilute salt solution. This is clearest at the end of the experiment, when the salt solution is injected after bleeding. The injection, diminishing considerably the percentage of organic substance in the saliva, diminishes somewhat the amount secreted in a given time, but not more than we should expect from the decrease in the strength of the stimulus.

This, taken with what has been said above on the secretion of water and of salts, indicates that *the secretion of organic substance depends wholly, or almost wholly, upon the strength of the stimulus, whilst the secretion of water and of salts depends also upon the amount of blood flowing through the gland.* The same result, although less conspicuously, follows the first injection; the percentage of organic substance in III. and IV. is much less than corresponds to the rate of secretion; the amount of organic substance secreted in a given time is greater than in I. and II., since more pilocarpin was injected, and thus the stimulus stronger.



## Experiment 9.

August 12, 1887. Dog. Weight 15 kilos. Vago-sympathetic cut.

	Number of c.c. of saliva collected.	Rate of secretion per min. in c.c.	Percentage of organic substance.	Percentage of salts.	Amount of organic substance in 100 min. in grams.	Amount of salts in 100 min. in grams.	Remarks.
I.	10.36-10.40	.750	.479	.413	.359	.310	10.34. Inject 5 mgrm. pilocarpin into jugular vein.
II.	10.42-10.51	.355	.416	.401	.148	.142	
III.	10.55-10.59	.825	1.570	.545	1.295	.450	Chorda stimulated, $c = 5$ .
IV.	11.6-11.11	.700	.865	.525	.606	.368	11.4. Inject 5 mgrm. pilocarpin.
V.	11.11-11.21	.490	.672	.515	.329	.252	11.25. Inject about 1 mgrm. atropin sulphate; secretion stops.
VI.	12.11-1.1	.124*	.619	.284	.077	.035	11.55. Inject 10 mgrm. pilocarpin; no secretion, nor on stimulating chorda.
VII.	1.31-2.13	.086	.148	.177	.013	.015	Chorda stimulated 30 sec. in each minute, $c = 0$ . 1.15-1.24. Inject 15 mgrm. pilocarpin.
VIII.	2.31-2.46	.207	.084	.134	.017	.028	2.20-2.28. Inject 560 c.c. NaCl .6 p.c. into jugular; drops increase from $1\frac{1}{2}$ to $3\frac{1}{2}$ a minute.
IX.	2.51-2.59 $\frac{1}{2}$	.747 .235	.181	.209	..	..	{ Chorda stimulated 9 times for 30 sec., with intervals of 30 sec., $c = 0$ .
X.	3.6-3.17	.327	.061	.153	.020	.050	

\* This rate of secretion is too high, since the secretion usually continued in the intervals of non-stimulation; on the other hand, stimulation gave occasionally a mere trace of saliva; the maximum number of drops in 30 sec. was 2.

In this experiment the injection of normal salt solution into the blood very considerably increases the rate of secretion of saliva, and this increase does not lead to any corresponding increase in the secretion of salts. Comparing salivas VII. and VIII., we see that, although in VIII. the secretion of saliva is more than twice as fast as in VII., yet it contains a *less* percentage of salts. And all three samples of saliva obtained after injection of normal salt solution have a much less percentage of salts than corresponds to their rate of secretion; this is readily seen when these samples are compared with those similarly obtained, but before injection, as in the following Table :—

TABLE X.

Number of sample.	Manner of producing secretion.	Rate of secretion.	Percentage of salts.
VI. IX.	<div> <div>Stimulate chorda</div> <div>after pilocarpin given</div> </div> <div> <div>— <i>before</i> injecting NaCl .6 .</div> <div>— <i>after</i> injecting NaCl .6 .</div> </div>	<div>·110 about</div> <div>·700 about</div>	<div>·2844</div> <div>·2092</div>
II. X.	<div> <div>Pilocarpin . . . .</div> </div> <div> <div>— <i>before</i> injecting NaCl .6 .</div> <div>— <i>after</i> injecting NaCl .6 .</div> </div>	<div>·355</div> <div>·327</div>	<div>·4008</div> <div>·1528</div>
VII. VIII.	<div> <div>Pilocarpin . . . .</div> </div> <div> <div>— <i>before</i> injecting NaCl .6 .</div> <div>— <i>after</i> injecting NaCl .6 .</div> </div>	<div>·086</div> <div>·206</div>	<div>·1772</div> <div>·1344</div>

At the same time, when the three samples of saliva obtained after the injection of salt solution are compared together, instead of with those obtained earlier, it is found that the percentage of salts in them follows HEIDENHAIN'S law.

Here, as in Experiment 8, the rate of secretion of organic substance does not increase to the extent that it normally would, with the increased rate of secretion of water.

#### EFFECT OF INJECTING INTO THE BLOOD A 2 PER CENT. SOLUTION OF $\text{Na}_2\text{CO}_3$ .

We have tried the effect of injecting a 2 per cent. solution of salt into the blood in one experiment only, but the result was quite decisive as regards one point: *the injection considerably increases the rate of secretion obtained by a stimulation of given strength of the chorda tympani*. The experiment was a continuation of 5a (*cf.* p. 123). Three samples of saliva were obtained, under normal conditions, by stimulating the chorda, the secondary coil being at 14; the rate of secretion varied from 1·4 to 1·8 c.c. in a minute. Then 250 c.c. of 2 per cent. solution of  $\text{Na}_2\text{CO}_3$  were injected into the blood; after this the chorda was again stimulated, the rate of secretion was 2·4 to 2·8 c.c. in a minute. Further injection of 500 c.c. of a solution containing 1 per cent. KI and 1 per cent. NaCl still left the rate of secretion, on chorda stimulation, higher than normal.

*Experiment 5b.*

For first part of the Experiment see 5a, p. 123. The saliva was obtained throughout by a single stimulation of the chorda,  $c = 14$ .

		Time of stimulation in minutes.	Amount of saliva collected in c.c.	Rate of secretion per minute in c.c.	Percentage of organic substance.	Percentage of salts.	Amount of organic substance in 100 minutes.	Amount of salts in 100 minutes.	Remarks.
VII.	1.34	1	2.8	2.8	.919	.699	2.5732	1.9572	1.24-1.33. Inject 250 c.c. 2 p.c. $\text{Na}_2\text{CO}_3$ into a branch of the jugular.
VIII.	1.35	$1\frac{1}{2}$	2.2	1.47	.847	.436	1.2451	.6409	These samples of saliva were obtained by a single stimulation, there being no break in the stimulation between the end of VII. and the beginning of VIII.
IX.	2.33	$1\frac{1}{4}$	3.0	2.4	.761	.501	1.8264	1.2024	
X.	2.53	$1\frac{1}{2}$	3.0	2.0	.772	.551	1.5440	1.1020	2.42-2.51. Inject 100 c.c. KI 1 p.c. + NaCl 1 p.c. Secretion becomes slower towards end.
XI.	3.10	$1\frac{1}{2}$	3.2	2.13	.584	.517	1.2439	1.1012	3.0-3.7. Inject 200 c.c. KI 1 p.c. + NaCl 1 p.c.
XII.	3.25	$1\frac{1}{2}$	3.2	2.13	.501	.467	1.0671	.9947	3.16-3.21. Inject 200 c.c. KI 1 p.c. + NaCl 1 p.c.

With regard to the effect of the injection of the sodium carbonate on the percentage of salts in the saliva, we have hardly the means of arriving at a well-grounded conclusion. If we take the percentage of salts in I., III., and VI. as a standard, allowing a slight increase in III. and VI. for the after-result of dyspnoea, it appears that the first saliva, VII., collected after injecting sodium carbonate solution, contains a higher percentage of salts than corresponds to its rate of secretion; that the second sample, VIII., collected immediately after VII., contains about a normal percentage; and the third, IX., collected after an interval of an hour, contains rather less than the normal percentage for its rate of secretion. The *rate* of secretion of organic substance, and of salts, as well as that of water, is increased, so that the injection rendered either the nerve or the gland more irritable. The first injection of potassium iodide with sodium chloride increases the percentage of salts; the subsequent two injections decrease the percentage of salts, the rate of secretion in all three being very nearly the same. The decrease in the percentage of salts is no doubt due to the poisonous action of the potassium iodide, but it is not as yet worth while to discuss the matter. We give the results as another proof of what we wish to show, viz., the partial independence between the secretion of water and the secretion of salts in saliva.

#### EFFECT OF INJECTING STRONG SALT SOLUTIONS INTO THE BLOOD.

Having found that the injection of dilute salt solution into the blood might lead to a decrease in the percentage of salts, with an increased rate of secretion, we expected that the injection of a strong salt solution would very considerably increase the percentage of salts in the saliva. We find, however, that, whilst injection of strong salt solutions increases the percentage of salts in saliva, the increase is small, considering the amount of salts injected.

## Experiment 10.

July 2, 1888. Dog. Weight 6 kilos. Chordo-lingual and vago-sympathetic cut on left side. Pilocarpin solution nominally\* .5 p.c.

	Time of secretion in minutes.	Amount of saliva collected in c.c.	Rate of secretion per minute in c.c.	Percentage of organic substance.	Percentage of salts.	Remarks.
I.	12.22½	1.6	.292	.347	.590	12.20. Inject 1 c.c. pilocarpin into right jugular. Secretion begins 6 drops, ends 4 drops, a minute.
II.	12.31	2.2	.085	.357	.281	Secretion begins 2 drops, ends 1 drop, a minute. 12.38-1.2. Inject 50 c.c. 20 p.c. NaCl solution into right jugular. 1.4. Inject 1 c.c. pilocarpin.
III.	1.11	2.5	.208	.310	.685	Secretion begins 4 drops, ends 2¼ drops, a minute.
IV.	1.27	1.4	.038	.608	.352	Secretion begins 1½ drops, falls slowly to ½ drop, a minute.

1.45. Inject .5 c.c. pilocarpin; rate of secretion increases to 1 drop a minute, in 5 min. falls to rather less than this.

2.4. Inject 10 c.c. NaCl 20 p.c. Respiration stops, but begins again after artificial respiration. Secretion very slow. Further injection of 3 c.c. of pilocarpin, 1 c.c. at a time, does not quicken the secretion. Injection of 350 c.c. NaCl .2 p.c. solution causes a slight quickening.

3.5. Stimulation of chorda has very little, if any, effect. After death, gland found to be a little cedematous.

\* The pilocarpin used in this experiment was not the pilocarpin nitrate used in the other experiments. In 1882, I received from Kew a packet of leaves from British Guiana, supposed to contain an alkaloid like pilocarpin. Messrs. BRADY and MARTIN treated the leaves in the usual manner for the extraction of alkaloids, and so obtained a small quantity of a brownish, rather viscous, substance. This was dissolved with the aid of a little acid to make a .5 p.c. solution. I found that the solution differed from pilocarpin in causing rather less secretion of saliva, less slowing of the heart, less fall of blood pressure, and in having a greater paralysing influence on the secretory fibres of the chorda tympani and on the inhibitory fibres of the vagus. The solution prepared in 1882, filtered from some fungus which had grown in it, was used in Experiment 10 (J. N. LANGLEY).

Here the injection into the blood of 10 grm. of sodium chloride, dissolved in 50 c.c. of water, increases in a marked but not immoderate degree the percentage of salt in the saliva. This is better seen by arranging the results in the following manner:—

TABLE XI.

		Rate of secretion per minute in c.c.	Percentage of salts.
I.	Saliva before injecting NaCl solution	·292	·590
III.	Saliva after injecting NaCl solution	·208	·685
II.	Saliva before injecting NaCl solution	·085	·281
IV.	Saliva after injecting NaCl solution	·038	·352

It will be noticed that the slow secretion (IV.) occurring after injection of the salt solution contains a comparatively high percentage of organic substance ; since there is reason to suppose that the strength of stimulus was less in this case than during the secretion of the saliva immediately before it, we take the increased percentage of organic substance to be due to a lessened secretion of water, brought about by the strong salt solution interfering with the blood flow through the gland. This, no doubt, also contributes towards increasing the percentage of salts in the saliva.

*Experiment 11.*

July 3, 1888. Dog. Weight,  $12\frac{1}{2}$  kilos. Chordo-lingual and vago-sympathetic cut on left side. Pilocarpin nitrate .2 per cent. Injection made into a branch of the crural artery peripherally.

	Time of secretion in minutes.	Amount of saliva in c.c.	Rate of secretion in c.c. per minute.	Percentage of organic substance.	Percentage of salts.	Remarks.
I.	12.36	2.8	.700	.325	.347	12.27-12.33 $\frac{1}{2}$ . Inject 5 mgrm. pilocarpin.
II.	12.43	2.7	.675	.344	.401	The rate of secretion falls unusually slowly.
III.	12.56	2.4	.800	.453	.612	12.50-12.54. Inject 50 c.c. NaCl 20 p.c.
IV.	1.4	3.4	.566	.416	.641	1.0-1.3. Inject 50 c.c. NaCl 20 p.c. The secretion becomes slower during the injection.
V.	1.20	0.8	.062	.924	.569	1.14-1.17. Inject 50 c.c. NaCl 20 p.c. The secretion becomes very slow during the injection.

1.33. Inject 2 mgrm. pilocarpin. The heart stops, or nearly so; recovers on artificial respiration; but, then, cannot get secretion of saliva by injecting pilocarpin, nor by stimulating the chorda. After death, the gland found to be distinctly oedematous.

The injection of strong sodium chloride solution into the blood causes here, as in the previous experiment, an increase in the percentage of salts in the saliva secreted, and, taking the rate of secretion into consideration, there is an increase in the percentage of salts after each injection. But in neither experiment does the percentage of salts reach the maximum ( $\cdot77$  to  $\cdot78$  per cent.) which may be obtained normally with a rapid secretion. It is possible, however, that, if a rapid secretion had been obtained, the normal maximum percentage of salts might have been exceeded.

According to KLIKOWICZ,\* the blood, when strong sodium chloride solution is injected into the circulation, very rapidly gives up sodium chloride to the tissues, and takes up water from them.† From these causes combined, but especially from the former, the injection of sodium chloride into the blood does not lead to a corresponding increase in the percentage of salts in it. Thus, KLIKOWICZ found that the injection of 21 grm. of NaCl—in 10 per cent. solution—into the blood of a Dog weighing 24·5 kilos. only increased the percentage of Cl in the blood from  $\cdot301$  to  $\cdot435$ , and in the serum from  $\cdot371$  to  $\cdot554$ ; the blood being taken two minutes after the end of the injection, which itself lasted five minutes. But the amount of NaCl injected, if simply added to the amount of blood in the animal, would increase the percentage of Cl in the blood by at least 1·2, if it all remained in the plasma, and by about half as much, if it were equally distributed between blood corpuscles and plasma.

In our experiments, about twice as much NaCl per kilo. of body weight was injected as in KLIKOWICZ'S experiments. By the light of KLIKOWICZ'S results we should suppose that in our experiments the percentage of salts in the plasma, during the collection of saliva, varied from 1 to 1·5 per cent.

In Experiment 11, the injection of strong salt solution not only increases the percentage of salts in the saliva, but also the percentage of organic substance; this is very markedly the case in V. In V. the small rate of secretion makes it unlikely that the salt solution exerts a stimulating action on the gland. An indirect action may take place by means of the blood vessels. The salt solution may diminish the normal blood flow through the gland, either by weakening the heart beat, or by counteracting the vaso-dilator effect of pilocarpin. And this would be sufficient to account for the rise in percentage of the organic substance, and for a part of the rise in percentage of the salts.

Since it seemed possible that a mixture of the various salts found in saliva might have a greater effect than sodium chloride alone, we tried one experiment, injecting into the blood a solution containing about 19 per cent. of the salts found in saliva, viz. :—

\* KLIKOWICZ, 'Archiv f. Anat. u. Physiol. (Physiol. Abth.),' 1886, p. 534.

† The injection of strong sodium chloride caused the sub-maxillary gland in both of our experiments to become somewhat oedematous.



	Per cent.
Sodium chloride . . . . .	7·730
Potassium chloride . . . . .	4·600
Sodium carbonate . . . . .	4·510
Potassium sulphate . . . . .	1·045
Calcium carbonate . . . . .	·750
Calcium phosphate . . . . .	·565
	<hr/> 19·200

CO<sub>2</sub> was passed through this to dissolve as far as possible the calcium salts, and the mixture was then filtered.

*Experiment 12.*

July 4, 1888. Dog. Weight,  $15\frac{1}{2}$  kilos. Chordo-lingual and vago-sympathetic cut. The pilocarpin nitrate was injected into a branch of the crural vein centrally; the salt solution was injected into a branch of the crural artery peripherally.

		Time of collecting saliva in minutes.	Amount of saliva collected.	Rate of secretion per minute in c.c.	Percentage of organic substances.	Percentage of salts.	Remarks.
I.	12.46	18	2.8	.156	.160	.213	12.42. Inject 3 mgrm. pilocarpin.
II.	1.6	2	3.0	1.500	.583	.600	1.4. Inject 3 mgrm. pilocarpin.
III.	1.10	5	2.5	.500	.273	.341	Secretion begins 10, and ends $5\frac{1}{2}$ drops a minute. 1.6-1.21 $\frac{1}{2}$ . Inject 50 c.c. solution of salts; this apparently delays the fall in the rate of secretion. Secretion begins $5\frac{1}{2}$ , and ends $5\frac{3}{4}$ drops a minute.
IV.	1.22	8	2.9	.362	.284	.355	1.31. Inject 2 mgrm. pilocarpin.
V.	1.33	2	2.4	1.200	.414	.522	1.49-1.52. Inject 50 c.c. solution of salts.
VI.	1.36	6	3.2	.533	.239	.385	2.2. Inject 2 mgrm. pilocarpin.
VII.	1.44	5	2.6	.520	.200	.340	Rate of secretion rapidly falls.
VIII.	1.54	7	3.1	.443	.160	.284	2.6. Inject 4 mgrm. pilocarpin; increases rate of secretion.
IX.	2.4	2	3.7	1.850	.512	.695	2.11. Inject 4 mgrm. pilocarpin; very slight effect on rate of secretion.
X.	2.8	2	3.3	1.650	.933	.713	2.18. Inject 8 mgrm. pilocarpin; slightly increases rate of secretion 3 minutes after injection.
XI.	2.14	3	3.2	1.067	.927	.509	
XII.	2.22	4	3.8	.950	1.408	.543	

In this experiment, we may take as normal the first three samples of saliva secreted under the influence of pilocarpin, before the solution of salts was injected, and compare with these the saliva secreted after the injection of salts. Samples X. and XII. we omit from the following Table, and consider them later (*cf.* p. 147), since we think that the percentage of salts in these was largely influenced by the considerable dose of pilocarpin given.

TABLE XII.

	Rate of secretion per minute in c.c.	Percentage of salts.	Variation in percentage of salts corresponding to a variation of .01 c.c. a minute in rate of secretion.	Remarks.
I.	.156	.213 }	.0037	Normal.
III.	.500	.341 }		
II.	1.500	.600 }	.0026	
†IV.	.362	.355 }	..	Immediately after injecting 50 c.c. 19 p. c. salts; percentage of salts in IV. much above normal.
III.	.500	.341 }		
†V.	1.200	.522 }	.0026	Percentage of salts in V. slightly higher than normal.
II.	1.500	.600 }		
III.	.500	.341 }	.0133	Percentage of salts in VI. above normal.
†VI.	.533	.385 }		
V.	.500	.341 }	..	Percentage of salts in VII. above normal, and more so than in VI.
†VII.	.520	.340 }		
†VIII.	.443	.284 }	.001	Immediately after injecting 50 c.c. 19 p. c. salts; percentage of salts in VIII. above normal, but less so than in VII.
III.	.500	.341 }		
II.	1.500	.600 }	.0027	Percentage of salts in IX. slightly above normal.
†IX.	1.850	.695 }		
†XI.	1.067	.509 }	.0021	Percentage of salts in XI. normal, or nearly so.
II.	1.500	.600 }		

It will be seen from the above Table that, of the three rapid secretions obtained after the injection of salts into the blood (V., IX., XI.), two (V. and IX.) have apparently a slightly higher percentage of salts than normal.

The slower secretions (IV., VI., VII., VIII.) have all a higher percentage of salts than normal, and this is very marked in IV., which was taken soon after injecting salts into the blood.

That is to say, *with an increase of salts in the blood which leaves the secretory power of the gland unaffected, the percentage of salts is relatively more increased with slowly secreted than with rapidly secreted saliva.*

The considerable increase in salts in IV. is, we think, due to some interference with the circulation through the gland, for this contains a higher percentage of organic substance than the more rapidly secreted saliva III.

#### GENERAL REMARKS ON THE EFFECT ON THE SECRETION OF SALTS AND INJECTING SALT SOLUTION INTO THE BLOOD.

We have seen that, when the volume of the blood is increased to any considerable extent by salt solution varying from .2 to 2 per cent., the rate of secretion for a given stimulus is increased. This we take to be due to a larger quantity of blood passing through the gland; and from this, together with the fact that bleeding decreases the rate of secretion, we conclude that, within certain limits, the amount of water secreted for a given stimulus—with a given irritability of the gland—varies directly with the amount of blood passing through the gland.

The increased secretion of water brought about by increased blood-flow is accompanied, unless, perhaps, when the blood is excessively diluted, by an increase in the secretion of salts. The extent of the increase depends upon the percentage of salts in the blood; if the percentage of salts in the blood be sufficiently diminished, the increase in the amount of salts secreted does not keep pace with the increase in the secretion of water, and, consequently, the percentage of salts in the saliva falls. If the percentage of salts in the blood be sufficiently increased, that of the saliva will also be increased.

We have made no direct experiments upon the effect of increasing the volume of the blood without altering the percentage of salts in it; but we are inclined to think, from a consideration of Experiment 4, that in such case, and with a given stimulus, the secretion of water would be more increased than the secretion of salts; that is, that the percentage of salts would increase with the increase of flow, but rather less than normally.

In Experiment 4, the saliva is obtained before and after giving a small dose of atropin. After such a dose, stimulation of the chorda tympani with strong induction shocks, or the injection of large doses of pilocarpin, produces on the gland the effect of a weak stimulus only, in so far that the secretion of water is slow, and the percentage of organic substance and of salts in it is small. But the stimuli are still able to produce a maximal, or nearly maximal, effect on the small arteries. Hence, then, in Experiment 4, the samples of saliva III. to VI. inclusive are obtained under conditions of more copious blood supply than normally accompanies a weak stimulation of the gland. Taking I. as a standard, we think that III. to VI. contain a smaller percentage of salts than corresponds with their rate of secretion.

#### VARIATION IN THE PERCENTAGE OF SALTS IN SALIVA SECRETED UNDER THE INFLUENCE OF PILOCARPIN.

In comparing samples of saliva secreted at different rates under the influence of pilocarpin, we, of course, leave out of account those in which one sample is secreted

before and another after bleeding, clamping the carotid, or other treatment which may modify the character of the saliva subsequently secreted. We take only those cases in which the two or more samples of saliva are obtained in succession by pilocarpin. The number of the sample of saliva will show whether it was secreted at the beginning of an experiment or not.

There are eight cases in which the saliva obtained by pilocarpin can be compared; in six of these the percentage of salts follows HEIDENHAIN'S law. In consequence of the effect of pilocarpin upon the heart and upon the small arteries, we should not expect to find that the statement we have made above with regard to chorda saliva—viz., that, with equal increments in the rate of secretion, the increments in the percentage of salts become less—should necessarily hold with regard to pilocarpin saliva. But five of the six cases which follow HEIDENHAIN'S law show more or less distinctly that the statement is also true, under certain conditions, with saliva obtained by pilocarpin.

TABLE XIII.

		Rate of secretion per minute in c.c.	Percentage of salts.	Increase in percentage of salts corresponding to an increase of .01 c.c. a minute in rate.	Weight of Dog in kilos.	Remarks.
Ex. 10.	II.	.085	.281	.0149	6	{ 3 mgrm. pilocarpin injected before I.
	I.	.292	.590			
Ex. 7.	XII.	.116	.424	.02	..	{ 4 mgrm. pilocarpin injected before X., 8 mgrm. before XI., 15 mgrm. before XII.
	X.	.125	.442			
	XI.	.192	.476			
Ex. 4.	V.	.182	.238	.0062	..	{ 7.5 mgrm. pilocarpin injected before V.
	IV.	.376	.358			
Ex. 12.	I.	.156	.213	.0037	15½	{ 3 mgrm. pilocarpin injected before I., and 3 mgrm. before II.
	III.	.500	.341			
	II.	1.500	.600			
Ex. 8.	II.	.250	.420	.0033	8¼	{ 3 mgrm. pilocarpin injected before I., and 3 mgrm. before III. The percentage of salts in II. may have been slightly diminished by the injection of NaCl .2 p. c. (cf. p. 22).
	I.	.675	.559			
	III.	1.650	.752			
Ex. 9.	II.	.355	.401	.0003	15	{ 5 mgrm. pilocarpin injected before I.
	I.	.750	.403			
	V.	.490	.515	.0005	..	{ 5 mgrm. pilocarpin injected before IV.
	IV.	.700	.525			

In Experiment 9, it is clear that the fall in the percentage of salts is too slow compared with the fall in the rate of secretion. The probable reason of this we will consider with the two cases in which the percentage of salts did not follow HEIDENHAIN'S law. These are—

TABLE XIV.

		Rate of secretion per minute in c.c.	Percentage of salts.	Weight of Dog in kilos.	Remarks.
Ex. 11.	I.	·700	·347	12½	{ 5 mgrm. pilocarpin injected before I.
	II.	·675	·401		
Ex. 12.	IX.	1·850	·695	15½	{ 2 mgrm. pilocarpin injected before IX., 4 mgrm. before X., 4 mgrm. before XI., 8 mgrm. before XII.
	X.	1·650	·713		
	XI.	1·067	·509		
	XII.	·950	·543		

The explanation of the variations found in experiments 9, 11, 12 we take to be that the pilocarpin did not bring about the normal increase in the blood flow through the gland. In the absence of direct observations on the blood flow in these cases, we cannot, of course, positively assert that the explanation we give is the true one, but there are certain facts somewhat in favour of it.

In Experiment 11, the rate of secretion of organic substance is rather faster in II. than in I. :—

TABLE XV.

	Amount of organic substance secreted in 100 min.
I.	·2275
II.	·2322

So that presumably the stimulus to the gland-cells either was a little stronger in II. than in I., or the gland had increased in irritability; but, since the rate of secretion of water was rather slower in II., despite this, it is probable that the blood flow through the gland was less in amount in II.

In Experiment 9, the salts fall with the falling secretion, but less than normally; but, since the percentage of organic substance also falls less than normally, the cause of the variation may be that the water is secreted less rapidly than corresponds with the strength of stimulus and a full blood flow; that is to say, the percentage of salts falls less than normally because the flow of blood through the gland falls more than normally.

Lastly, we have to consider the exceptions from HEIDENHAIN'S law in Experiment 12. If we compare the percentage of salts in IX. and XI. with that in II., we see that

both contain very nearly a normal percentage of salts, it being, we think, a trifle higher than normal in IX. on account of the injection of salts taking place shortly before (*cf.* p. 142). The exceptions to the law are X. and XII.

Taking the rate of secretion of organic substance in IX. to XII., we have :—

TABLE XVI.

	Amount of organic substance secreted in 100 min.
IX.	·9472
X.	1·5394
XI.	·9891
XII.	1·3376

*i.e.*, the stimulus to the gland, as indicated by the rate of secretion of organic substance, was considerably greater in X. and XII. than in IX. and XI. In X., notwithstanding the stronger stimulus, less water is secreted than in IX.; probably, then, during the secretion of saliva X. less blood was flowing through the gland. And this is the more likely in this instance, for, when successive doses of pilocarpin are injected into the blood, they produce less and less increase of the blood flow through the gland.\* But, as we have seen, a decreased flow of blood during an increased stimulus is adequate to cause an increase in the percentage of salts. A similar line of argument applies to XI. and XII.

A comparison of IX. and XII. shows that there remains an intimate connection between the percentage of salts and the rate of secretion of water, for XII. secreted, if the foregoing reasoning is sound, under the influence of a stronger stimulus than IX. and with less blood flow, and in consequence, having a higher percentage of salts than normal, has nevertheless a considerably lower percentage of salts than IX., which is secreted at a rapid rate.

We may consider here one or two other results bearing on this question. In Experiment 7 (X. to XII.), increasing the quantity of pilocarpin given, increases the rate of secretion of organic substance very much more than it increases the rate of secretion of water or of salts. When a fairly large dose of pilocarpin is given at the beginning of an experiment, a rapid secretion of saliva takes place and the percentage of organic substance in it is high. Subsequent doses produce a less and less rapid secretion of saliva; so that, although the percentage of organic substance remains high, the rate of secretion of organic substance much diminishes. At the same time, there is a great decrease in the irritability of the chorda tympani, shown by the fact that electrical stimulation of the chorda tympani has very little

\* LANGLEY, 'Journal of Anat. and Physiol.,' vol. 11, 1876, p. 176; and 'Journal of Physiology,' vol. 1, 1878, p. 366.

effect. It follows from this, since there is good ground for supposing that pilocarpin causes a secretion by stimulating the endings of the chorda tympani, that pilocarpin also is unable to stimulate strongly the gland. The high percentage of organic substance, then, in the saliva secreted slowly after repeated doses of pilocarpin must in the main be referred to the diminished blood supply to the gland. And it is probable that the percentage of salts in the saliva, though higher than normal, is not very greatly so, because the stimulus to the gland is far from the normal maximum. In this way we should explain the results of Experiment 7, X. to XII.

An instance of an increase in the percentage of salts caused directly by an increased stimulus, and not indirectly by increasing the rate of secretion of water, is, perhaps, given in Experiment 4. In sample VI., stimulation of the chorda has, in consequence of the previously injected atropin and pilocarpin, a barely appreciable effect on the rate of secretion of water, but it increases the percentage of organic substance and of salts above that of V., secreted previously to, and at the same rate as, VI.

#### THE EFFECT OF A SMALL DOSE OF ATROPIN UPON THE PERCENTAGE COMPOSITION OF SALIVA.

It has been argued by one of us\* that atropin paralyses “secretory” and “trophic” fibres simultaneously. The results of Experiments 4 and 9 offer some confirmation of this.

In both of these experiments a small dose of atropin is given, such that a stimulation of the chorda and injection of pilocarpin still produce some secretion. If atropin affected the “secretory” before the “trophic” fibres, the saliva obtained after atropin has been given should contain a high percentage of organic substance in proportion to its rate of secretion. This is not the case; on the contrary, the percentage of organic substance is small; the percentage is, in fact, so small that it, at first sight, appears as if the “trophic” fibres were affected more than the “secretory” fibres by the atropin. But we have seen that the secretion of water depends in part upon the amount of blood flow through the gland. In these experiments, after atropin had been given, the stimulation of the chorda and the injection of pilocarpin caused a copious blood flow, with but slight activity of the gland cells; hence, the secretion of water was abnormally increased.

#### SUB-LINGUAL SALIVA.

WERTHER† has shown that the sub-lingual saliva of the Dog contains a very high percentage of salts, and a rather low percentage of organic substance. The three analyses given by him are as follows:—

\* LANGLEY, ‘Journal of Physiology,’ vol. 9, 1888, p. 55.

† WERTHER, ‘Archiv. f. d. ges. Physiol.,’ vol. 38, 1886, p. 298.



TABLE XVII.

	Percentage of organic substance.	Percentage of salts.	Percentage of solids.
I.	·19	1·34	1·53
II.	·43	·94	1·37
III.	·34	·94	1·28

Since WERTHER'S are the only observations on the subject, we collected the saliva secreted by the left sub-lingual gland during the course of Experiment 12. In about  $1\frac{3}{4}$  hour, 2·6 c.c. of saliva were secreted. This was analysed, with the following result :—

TABLE XVIII.

Percentage of organic substance.	Percentage of salts.	Percentage of solids.
·602	1·034	1·636

The result confirms WERTHER'S observations as to the high percentage of salts ; the percentage of organic substance is, however, somewhat higher than in his analyses. In the course of our experiment, 19 grm. of salts were injected into the blood ; this, taken in conjunction with WERTHER'S observations, shows that the injection into the blood of a considerable amount of salts has very little effect upon the secretion of salts by the sub-lingual gland.

#### THE RAPIDITY OF SECRETION OF CERTAIN SALTS WHEN INJECTED INTO THE BLOOD.

We have tried also two experiments on the rapidity with which substances injected into a vein appear in the saliva. In these experiments pilocarpin was injected with the substances to be observed, and each successive three drops of saliva secreted collected separately and tested. We found that :

1. On injection of 50 c.c. of lithium citrate into the blood, the first drop secreted, both from the sub-maxillary and from the parotid gland, showed the lithium band in the spectroscope.
2. On injection of 50 c.c. of potassium iodide into the blood, this salt was present in all the drops of saliva after the first six. The potassium iodide was first detected in the sub-maxillary saliva, as the secretion from this gland was more rapid than that from the parotid. The presence of potassium iodide was observed by adding to the saliva a little starch solution and then a drop or two of strong nitric acid. There may, of course, have been traces of potassium iodide in the first drops of saliva, which this test failed to show.

3. The excretion of the salts injected continued during the whole of the experiment—two to three hours.
4. For a given amount of saliva, the parotid secreted more potassium iodide than the sub-maxillary gland.
5. On injecting potassium ferrocyanide 1 per cent. into the blood, no trace of it could at any time be found in the saliva.
6. On injecting sulphindigotate of soda into the blood, no indigo white could be found in the saliva. We tried this because it seemed possible that the known absence of sulphindigotate of soda from the salivary secretion, after copious injection of it into the blood, might be due to its conversion into indigo-white.

THE RECENT OBSERVATIONS OF NOVI.—After we had completed our experiments and nearly finished our account of them, we received a separate copy of a paper by NOVI on the effect of injecting a strong solution of sodium chloride into the blood on the percentage of chlorine in saliva.

NOVI's observations, undertaken at the suggestion of LUDWIG, were made on Dogs, and in the following manner:—About 80 c.c. of blood were withdrawn from the Dog, then saliva collected; after this a 10 per cent. solution of salt was injected into the blood, a fresh sample of saliva collected, and a further portion of blood withdrawn. This was repeated one or more times, according to the weight of the animal and the freedom of secretion of saliva. The percentage of chlorine in the several samples of blood serum and of saliva was then determined. The chief results obtained were:

1. That an increase of chlorine (as chlorides) in the blood plasma increases the percentage of chlorine in the saliva with a given rate of secretion, and may increase it with a slower rate of secretion.
2. That with a rapid rate of secretion an increase of chlorine in the blood plasma may increase the percentage of chlorine in the saliva above the maximum that can normally be obtained.

With the former of these results our observations are in the main in agreement, but we find that an increase in the salts in plasma which does not interfere with the secretory power of the gland has very little effect on the percentage of salts in saliva as long as the secretion of water is rapid, and that the increase in the percentage of salts which take place with a slower secretion is partly due to the injection of strong salt solution leading to a decreased blood flow through the gland (*cf.* p. 136, *et seq.*).

The latter of these results, our observations leave undecided. For, whilst, on the one hand, we never obtained after injection of salts into the blood so high a percentage of salts in the saliva as can be obtained normally, on the other, we only once obtained a rapid secretion (Experiment 12, IX.) after the injection of salts; and it is possible that in this case the rate of secretion was less than the maximum, and that an insufficient amount of salts was injected.

At the same time, it may be pointed out that NOVI observed an increase above normal in the percentage of chlorine in saliva in three cases only, and these only slightly exceed the maximum known to occur in normal saliva. The maximum found by WERTHER in normal saliva is .352 per cent.; in the three cases of NOVI, mentioned above, the percentages of chlorine are .360, .363, .382, and NOVI mentions that the error in estimation of the chlorine may be as much as .03 per cent.

NOVI also found that, when the chlorine in serum was increased to .7 per cent., no more saliva could be obtained from the gland. His method of obtaining saliva was to place dilute acids or weak ammonia in the mouth, and so to set up a secretion reflexly. In our Experiments 10 and 11, the injection of strong salt solution distinctly lowers the amount of saliva that could be obtained from the gland by stimulating the chorda tympani and by pilocarpin, and, when injected in sufficient amount, prevented all secretion from taking place. Hence, it seems to us probable that, if the injection of salts can lead to an increase in the percentage of salts in the saliva above normal, the amount of salts injected must be regulated with great nicety.

#### SOME REMARKS ON THE THEORY OF SECRETORY NERVES.

We do not propose to discuss the question whether there is more than one kind of secretory nerve; but there are some facts in the foregoing experiments bearing on the question which we cannot leave without mention.

The most striking of these is the effect of bleeding in Experiment 8. The loss of blood causes an increase in the percentage of organic substance in the saliva.\* This tends to show that with a given stimulus the percentage of organic substance increases as the blood-flow through the gland decreases. Further, the actual rate of secretion of organic substance is somewhat decreased by loss of blood, and this may be fairly interpreted as meaning that with a lessened blood supply the gland-cells become less irritable. Lastly, loss of blood increases the percentage of salts much less than it increases the percentage of organic substance; that is to say, the secretion of salts is much less affected by the strength of stimulus than the secretion of organic substance.

Hence, it would appear that with a given stimulus to the gland-cells a decrease in

\* Since writing this we have met with an observation of ZERNER ('Medizinische Jahrbücher,' 1887, p. 534) bearing on the secretion of organic substance. He finds in the Dog that, after lowering the blood pressure by section of the cervical spinal cord, the more slowly secreted sub-maxillary saliva, obtained by stimulating the chorda tympani, has a higher percentage of organic substance than the more rapidly secreted saliva, similarly obtained under normal conditions. Two experiments are given. One of these is inconclusive, since the sympathetic was stimulated before obtaining the second sample of chorda saliva, and this, as HEIDENHAIN has shown, is sufficient to increase the percentage of organic substance. The other experiment, although more satisfactory, is not entirely so, for the chorda tympani was stimulated with strong shocks between the time of collecting the two samples of saliva analysed.—Feb. 6, 1889.

the blood-flow through the gland will lead to a diminished irritability of the gland, and, therefore, to a decrease in the rate of secretion of all the constituents of saliva. It will lead also directly to a considerable decrease in the secretion of water, to a less decrease in the secretion of salts, and to a still less decrease in the secretion of organic substance. With decreased blood-flow there will be less saliva, and this will contain a somewhat higher percentage of salts and a considerably higher percentage of organic substance. Further, with a given decrease of blood-flow, the stronger the stimulus, the higher will be the percentage of organic substance and of salts.

Now, sympathetic saliva is just such saliva as, from the above-mentioned facts and deductions, we should expect to be produced by simultaneous stimulation of a secretory nerve and of glandular vaso-constricted fibres. Since the decrease in the blood-flow through the gland is much greater on stimulating the sympathetic than on bleeding, the sympathetic saliva should be secreted more slowly and contain a higher percentage of organic substance than saliva secreted after bleeding. And this is the case.

That the effect of decreasing the blood-flow through the gland is as we have given it, is supported by several other experiments besides the one we have quoted here; but we do not enter into the matter further, for two reasons—the one that there are certain of HEIDENHAIN'S observations which appear to be contradictory to ours, and these we have not yet repeated; and the other that, since in the Cat stimulation of the sympathetic gives a saliva containing a low percentage of organic substance, it is desirable to investigate what in this case is the effect of a decreased blood flow.

#### SUMMARY OF CHIEF RESULTS.

HEIDENHAIN has shown that, when saliva is obtained by stimulating the chorda tympani, the percentage of salts in the saliva depends upon the rate of secretion; so that, the faster the secretion, the higher the percentage of salts is up to a limit of about '6 per cent. WERTHER has come to the same conclusion, but finds that the percentage of salts may be as much as '77.

In both HEIDENHAIN'S and WERTHER'S experiments there are a considerable number of exceptions to this rule, attributed by them to variations in the rate of secretion of saliva during the time of collecting any one sample.

We have repeated, with some modifications, the experiments of HEIDENHAIN, paying especial attention to the rate of secretion of the saliva, and find, in 10 out of 11 cases, that his law of an increase in the percentage of salts with an increase in the rate of secretion holds. The single exception may possibly be due to a modification in the blood-flow through the gland during the time of collecting the saliva. The slowly secreted saliva contains a low percentage of salts, whether it is produced by a weak

nerve stimulus, or by a very strong nerve stimulus, which lowers the irritability of the nerve-fibres.

We do not find any rate of secretion beyond which an increase in rate fails to increase the percentage of salts in the saliva. The increment in the percentage of salts decreases with each equal successive increment in the rate of secretion.

As a rule, in saliva obtained by injecting pilocarpin, the percentage of salts follows HEIDENHAIN'S law. We take the exception to be due to the action of pilocarpin on the circulation, the blood-flow through the gland being less than normally accompanies the degree of stimulation of the gland-cells.

The percentage of salts in saliva obtained by stimulating the sympathetic is higher than corresponds to its rate of secretion, the saliva obtained by stimulating the chorda being taken as a basis of comparison.

Dyspnœa decreases the rate of secretion of saliva, and, if not too prolonged, increases the percentage of salts, and tends to increase the percentage of organic substance in the saliva. This holds, whether the saliva be obtained by stimulating the chorda tympani, or by injecting pilocarpin. Dyspnœa has for a short time an after-action, tending to increase the percentage of salts, and possibly that of organic substance.

Clamping the carotid during secretion has the same general effect as dyspnœa, but it causes a still more marked increase in the percentage of salts. Its after-effect is also much greater and lasts longer. Bleeding has a similar effect to dyspnœa and to clamping the carotid, and it causes a marked increase in the percentage of organic substance.

Injection of dilute salt solution in sufficient quantity considerably increases the rate of secretion of saliva; the percentage of salts in the saliva decreases, although the rate of secretion of salts usually increases; the percentage of organic substance decreases—that is, increasing the volume of the blood with dilute salt solution chiefly increases the rate of secretion of water.

The percentage of salts in samples of saliva obtained *after* the injection of dilute salt solution increases with the rate of secretion; it is only when these are compared with samples obtained before the injection that a discrepancy in the normal relation between percentage of salts and rate of secretion of water appears.

Injection of sodium carbonate 2 per cent. also increases the rate of secretion of saliva; in this case the percentage of salts is about normal; the percentage of organic substance falls slightly only.

Injection of strong salt solution increases the percentage of salts in saliva; this is in accordance with the recent observations of NOVI, that the chlorine in the salts of saliva is increased for a given rate of secretion by increasing the percentage of sodium chloride in the blood. We find, however, that on injection of strong salt solution into the blood which leaves the secretory power of the gland unaffected, the increase in the percentage of salts is much greater with slowly than with rapidly secreted saliva, and that, when the secretory power of the gland is affected by the strong salt solution an increase in the percentage of organic substance also takes place; this and

a part of the increase in the percentage of salts we attribute to a decrease of the blood-flow through the gland.

Saliva produced by stimulating the chorda tympani or by injecting pilocarpin, after a small dose of atropin has been given, contains a low percentage of organic substance and of salts.

We, like WERTHER, find that sub-lingual saliva has a considerably higher percentage of salts than sub-maxillary saliva.

If lithium citrate, potassium iodide, potassium ferrocyanide, and pilocarpin are injected into the blood, lithium can be detected in the first drop of saliva secreted, iodine after the first six drops; potassium ferrocyanide cannot be detected at any stage of secretion.